Potential bioterrorism agent: Category A

PLAGUE

DISEASE REPORTING

In Washington

Since 1907 only one case of human plague has been reported in Washington, occurring in an animal trapper in 1984 in bubonic form.

Potential reservoirs for plague in Washington include wild animals, however cases are most likely to be travel-related. One case of pneumonic plague without travel to an endemic area may indicate an act of terrorism and constitute a public health emergency.

Purpose of reporting and surveillance

- To identify sources of transmission US (e.g., wild rodents or other animals) and to prevent further transmission from such sources.
- To identify sources of transmission and geographical areas of risk outside of the US.
- To raise the index of suspicion of a possible bioterrorism event if no natural exposure source is identified.
- To better characterize the epidemiology of this organism.

Reporting requirements

- Health care providers: **immediately notifiable to Local Health Jurisdiction**
- Hospitals: **immediately notifiable to Local Health Jurisdiction**
- Laboratories: **immediately notifiable to Local Health Jurisdiction**; specimen submission required
- Local health jurisdictions: notifiable to DOH Communicable Disease Epidemiology within 7 days of case investigation completion or summary information required within 21 days. ***If bioterrorism is suspected, case must be immediately reported to DOH: 1-877-539-4344***

CASE DEFINITION FOR SURVEILLANCE

Clinical criteria for diagnosis

Plague is transmitted to humans by fleas or by direct exposure to infected tissues or respiratory droplets; the disease is characterized by fever, chills, headache, malaise, prostration, and leukocytosis that manifests in one or more of the following principal clinical forms:

- Regional lymphadenitis (bubonic plague)
- Septicemia without an evident bubo (septicemic plague)
- Plague pneumonia, resulting from hematogenous spread in bubonic or septicemic cases (secondary pneumonic plague) or inhalation of infectious droplets (primary pneumonic plague)
- Pharyngitis and cervical lymphadenitis resulting from exposure to larger infectious droplets or ingestion of infected tissues (pharyngeal plague).

Laboratory criteria for diagnosis

Presumptive

- Elevated serum antibody titer(s) to *Yersinia pestis* fraction 1 (F1) antigen (without documented fourfold or greater change) in a patient with no history of plague vaccination, or
- Detection of F1 antigen in a clinical specimen by fluorescent assay.

Confirmatory

- Isolation of *Y. pestis* from a clinical specimen, or
- Fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen.

Case definition

- Probable: a clinically compatible case with presumptive laboratory results.
- Confirmed: a clinically compatible case with confirmatory laboratory results.

A. DESCRIPTION

1. Identification

A specific zoonosis involving rodents and their fleas, which transfer the bacterial infection to various animals and to people. Initial signs and symptoms may be nonspecific with fever, chills, malaise, myalgia, nausea, prostration, sore throat and headache. Commonly a lymphadenitis develops in those lymph nodes that drain the site of the flea bite, where there may be an initial lesion. This is bubonic plague, and it occurs more often in lymph nodes in the inguinal area (90%) and less commonly in those in the axillary and cervical areas. The involved nodes become swollen, inflamed and tender and may suppurate. Fever is usually present. All forms, including instances in which lymphadenopathy is not apparent, may progress to septicemic plague with bloodstream dissemination to diverse parts of the body, that include the meninges. Endotoxic shock and disseminated intravascular coagulation (DIC) may occur without localizing signs of infection. Secondary involvement of the lungs results in pneumonia; mediastinitis or pleural effusion may develop. Secondary pneumonic plague is of special significance, since respiratory droplets may serve as the source of person to person transfer with resultant primary pneumonic or pharyngeal plague; this can lead to localized outbreaks or devastating epidemics. Though naturally acquired plague usually presents as bubonic

plague, purposeful aerosol dissemination as a result of biowarfare or a terrorist event would be manifest primarily as pneumonic plague.

Untreated bubonic plague has a case-fatality rate of about 50%-60%. Plague organisms have been recovered from throat cultures of asymptomatic contacts of pneumonic plague patients. Untreated primary septicemic plague and pneumonic plague are invariably fatal. Modern therapy markedly reduces fatality from bubonic plague; pneumonic and septicemic plague also respond if recognized and treated early. However, patients who do not receive adequate therapy for primary pneumonic plague within 18 hours after onset of respiratory symptoms are not likely to survive.

Visualization of characteristic bipolar staining, safety pin ovoid, gram-negative organisms in direct microscopic examination of material aspirated from a bubo, sputum or CSF is suggestive, but not conclusive, evidence of plague infection. Examination by FA test or antigen capture ELISA is more specific and is particularly useful in sporadic cases. Diagnosis is confirmed by culture and identification of the causal organism from exudate aspirated from buboes, from blood, CSF or sputum, or by a fourfold or greater rise or fall in antibody titer. Slow growth of the organism at normal incubation temperatures may lead to misidentification by automated systems. The passive hemagglutination test (PHA) using *Y. pestis* Fraction-1 antigen is most frequently used for serodiagnosis. Medical personnel should be aware of areas where the disease is endemic and entertain the diagnosis of plague early; unfortunately, plague is often misdiagnosed, especially in travelers who develop illness after returning from an endemic area.

2. Infectious Agent

Yersinia pestis, the plague bacillus.

3. Worldwide Occurrence

Plague continues to be a threat because of vast areas of persistent wild rodent infection; contact of wild rodents with domestic rats occurs frequently in some enzootic areas. Wild rodent plague exists in the western half of the US; large areas of South America; north central, eastern and southern Africa; central and southeast Asia, and extreme southeastern Europe near the Caspian Sea. There are several natural plague foci within the Russian Federation and Kazakhstan. While urban plague has been controlled in most of the world, human plague has occurred in the 1990s in several African countries that include Botswana, Kenya, Madagascar, Malawi, Mozambique, Tanzania, Uganda, Zambia, Zimbabwe, and Democratic Republic of the Congo. Plague is endemic in China, Laos, Mongolia, Myanmar (Burma), India and especially in Vietnam where thousands of cases of bubonic plague, both urban and rural, with scattered outbreaks of pneumonic plague, were reported between 1962 and 1972. In the Americas, foci in northeastern Brazil and the Andean region (Peru, Ecuador and Bolivia) continue to produce sporadic cases and occasional outbreaks including an outbreak of pneumonic plague in Ecuador in 1998.

Human plague in the western US is sporadic, with only single cases or small common source clusters in an area, usually following exposure to wild rodents or their fleas. Over the 10 year period 1987-1996, there was an annual average of 10 plague cases (range 2 to 15). No human to human transmission has occurred in the US since 1925, although secondary plague pneumonia has occurred in about 20% of bubonic cases in recent years. Seventeen cases of primary plague pneumonia were acquired from pet cats with plague pneumonia in the interval 1977-1994.

4. Reservoir

Wild rodents (especially ground squirrels) are the natural vertebrate reservoir of plague. Lagomorphs (rabbits and hares), wild carnivores and domestic cats may also be a source of infection to people. Though the organism may remain viable for several weeks in water and moist meals and grains, it is killed with several hours of exposure to sunlight.

5. Mode of Transmission

Naturally acquired plague in people occurs as a result of human intrusion into the zoonotic (also termed sylvatic or rural) cycle during or following an epizootic, or by the entry of sylvatic rodents or their infected fleas into man's habitat with infection in commensal rodents and their fleas; this may result in the development of a domestic rat epizootic and epidemic plague. Domestic pets, particularly house cats and dogs, may carry plague infected wild rodent fleas into homes, and cats may occasionally transmit infection by their bites or scratches; cats develop plague abscesses that have been a source of infection to veterinarians.

The most frequent source of exposure that results in human disease worldwide has been the bite of infected fleas (especially *Xenopsylla cheopis*, the oriental rat flea). Other important sources include the handling of tissues of infected animals, especially rodents and rabbits, but also carnivores; rarely airborne droplets from human patients or household cats with plague pharyngitis or pneumonia; or careless manipulation of laboratory cultures. In a bioterrorist setting plague bacilli would probably be transmitted as an aerosol. Person to person transmission by *Pulex irritans* fleas, the “human” flea, is presumed to be important in the Andean region of South America and in other places where plague occurs and this flea is abundant on domestic animals. Certain occupations and lifestyles (including hunting, trapping, cat ownership and rural residence) carry an increased risk of exposure.

6. Incubation period

From 1 to 7 days; may be a few days longer in immunized individuals. For primary plague pneumonia, 1-4 days, usually short.

7. Period of communicability

Fleas may remain infective for months under suitable conditions of temperature and humidity. Bubonic plague is not usually transmitted directly from person to person unless

there is contact with pus from suppurating buboes. Pneumonic plague may be highly communicable under appropriate climatic conditions; overcrowding facilitates transmission.

8. Susceptibility and resistance

Susceptibility is general. Immunity after recovery is relative; it may not protect against a large inoculum.

B. METHODS OF CONTROL

1. Preventive measures:

The basic objective is to reduce the likelihood of people being bitten by infected fleas, having direct contact with infective tissues and exudates, or of being exposed to patients with pneumonic plague.

a. Educate the public in enzootic areas on the modes of human and domestic animal exposure; the importance of rat proofing buildings, preventing access to food and shelter by peridomestic rodents through appropriate storage and disposal of food, garbage and refuse; and the importance of avoiding flea bites by use of insecticides and repellents. In sylvatic or rural plague areas, the public should be advised to use insect repellents and warned not to camp near rodent burrows and to avoid handling of rodents, but to report dead or sick animals to health authorities or park rangers. Dogs and cats in such areas should be treated periodically with appropriate insecticides.
b. Survey rodent populations periodically to determine the effectiveness of sanitary programs and to evaluate the potential for epizootic plague. Rat suppression by poisoning (see B2f, below) may be necessary to augment basic environmental sanitation measures; rat control should always be preceded by measures to control fleas. Maintain surveillance of natural foci by bacteriologic testing of sick or dead wild rodents and by serologic studies of wild carnivore and outdoor ranging dog and cat populations in order to define areas of plague activity. Collection and testing of fleas from wild rodents and their nests or burrows may also be appropriate.
c. Control rats on ships and docks and in warehouses by rat proofing or periodic fumigation, combined when necessary with destruction of rats and their fleas in vessels and in cargoes, especially containerized cargoes, before shipment and on arrival from plague endemic locations.
d. Wear gloves when hunting and handling wildlife.
e. Active immunization with a vaccine of killed bacteria confers some protection against bubonic plague (but not primary pneumonic plague) in most recipients for at least several months when administered in a primary series of 3 doses with doses 1 and 2 1-3 months apart followed by dose 3 5-6 months later; booster injections are necessary every 6 months if high risk exposure continues. After the third booster dose, the intervals can be extended to every 1 to 2 years. Immunization of visitors to epidemic localities and of laboratory and field workers handling plague bacilli or

infected animals is justifiable but should not be relied upon as the sole preventive measure. Routine immunization is not indicated though for most persons living in enzootic areas such as the western US. Live attenuated vaccines are used in some countries, but may produce more adverse reactions and there is no evidence that they are more protective.

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority. Because of the rarity of naturally acquired primary plague pneumonia, even a single case should initiate prompt consideration by both public health and law enforcement authorities of a bioterrorist/biowarfare exposure.
b. Isolation: Rid patients, and especially their clothing and baggage, of fleas using an insecticide effective against local fleas and known to be safe for people; hospitalize if practical. For patients with bubonic plague (if there is no cough and the chest x-ray is negative) drainage and secretion precautions are indicated for 48 hours after start of effective therapy. For patients with pneumonic plague, strict isolation with precautions against airborne spread is required until 48 hours of appropriate antibiotic therapy have been completed and there has been a favorable clinical response (see B2g, below).
c. Concurrent disinfection: Of sputum and purulent discharges and articles soiled therewith. Terminal cleaning. Bodies of people and carcasses of animals that died of plague should be handled with strict aseptic precautions.
d. Quarantine: Those who have been in household or face to face contact with patients with pneumonic plague should be provided chemoprophylaxis (see B2e, below) and placed under surveillance for 7 days; those who refuse chemoprophylaxis should be maintained in strict isolation with careful surveillance for 7 days.
e. Protection of contacts: In epidemic situations where human fleas are known to be involved, contacts of bubonic plague patients should be disinfested with an appropriate insecticide. All close contacts should be evaluated for chemoprophylaxis. Close contacts of confirmed or suspected plague pneumonia cases (including medical personnel) should be provided with chemoprophylaxis using tetracycline (15-30 mg/kg) or chloramphenicol (30 mg/kg) daily in 4 divided doses for 1 week after exposure ceases.
f. Investigation of contacts and source of infection: Search for people with household or face to face exposure to pneumonic plague, and for sick or dead rodents and their fleas. Flea control must precede or coincide with antirodent measures. Dust rodent runs, harborages and burrows in and around known or suspected plague areas with an insecticide labeled for flea control and known to be effective against local fleas. If nonburrowing wild rodents are involved, insecticide bait stations can be used. If urban rats are involved, disinfest by dusting the houses, outhouses and household furnishings; dust the bodies and clothing of all residents in the immediate vicinity. Suppress rat populations by well-planned and energetic campaigns of poisoning and with vigorous concurrent measures to reduce rat harborages and food sources.
g. Specific treatment: Streptomycin is the drug of choice, gentamicin can be used when streptomycin is not readily available; tetracyclines and chloramphenicol are alternative choices. Chloramphenicol is required for treatment of plague meningitis.

All are highly effective if used early (within 8-18 hours after onset of pneumonic plague). After a satisfactory response to drug therapy, reappearance of fever may result from a secondary infection or a suppurative bubo that may require incision and drainage. See also: Inglesby TV, Dennis DT, Henderson DA, et al. Plague as a biological weapon: medical and public health management. JAMA 2000 May 3;283(17):2281-90 (in *Additional Resources*).

3. Epidemic measures

a. Investigate all suspected plague deaths with autopsy and laboratory examinations when indicated. Develop and carry out case finding. Establish the best possible facilities for diagnosis and treatment. Alert existing medical facilities to report cases immediately and to use full diagnostic and therapeutic services.
b. Attempt to mitigate public hysteria by appropriate informational and educational releases through the press and news media.
c. Institute intensive flea control in expanding circles from known foci.
d. Implement rodent destruction within affected areas only after satisfactory flea control has been accomplished.
e. Protect all contacts as noted in B2e, above.
f. Protect field workers against fleas; dust clothing with insecticide powder and use insect repellents daily.

4. International measures

a. Telegraphic notification within 24 hours by governments to WHO and to adjacent countries of the first imported, first transferred or first nonimported case of plague in any area previously free of the disease. Report newly discovered or reactivated foci of plague among rodents.
b. Measures applicable to ships, aircraft and land transport arriving from plague areas are specified in International Health Regulations. These regulations are being revised, but the new regulations will not be in effect until the year 2002 or after.
c. All ships should be free of rodents or periodically deratted.
d. Rat proof buildings at seaports and airports; apply appropriate insecticide; eliminate rats with effective rodenticide.
e. For international travelers, international regulations require that prior to their departure on an international voyage from an area where there is an epidemic of pulmonary plague, those suspected of significant exposure shall be placed in isolation for 6 days after last exposure. On arrival of an infested or suspected infested ship, or an infested aircraft, travelers may be disinfected and kept under surveillance for a period of not more than 6 days from the date of arrival. Immunization against plague cannot be required as a condition of admission to a territory.
f. WHO Collaborating Centres.

5. Bioterrorism measures

Y. pestis is distributed worldwide; techniques for mass production and aerosol dissemination are available; and the fatality rate of primary pneumonic plague is high and there is a real potential for secondary spread. For these reasons, a biological attack with plague is considered to be of serious public health concern. A few sporadic cases will likely be missed or at least not attributed to a deliberate bioterrorist act. Any suspect case of plague should be reported immediately by telephone to the local health department. The sudden appearance of many patients presenting with fever, cough, a fulminant course and high case-fatality rate should provide a suspect alert for anthrax or plague; if cough is primarily accompanied by hemoptysis, this presentation favors the tentative diagnosis of pneumonic plague. For a suspected or confirmed outbreak of pneumonic plague, follow the treatment and containment measures outlined in B2 above.